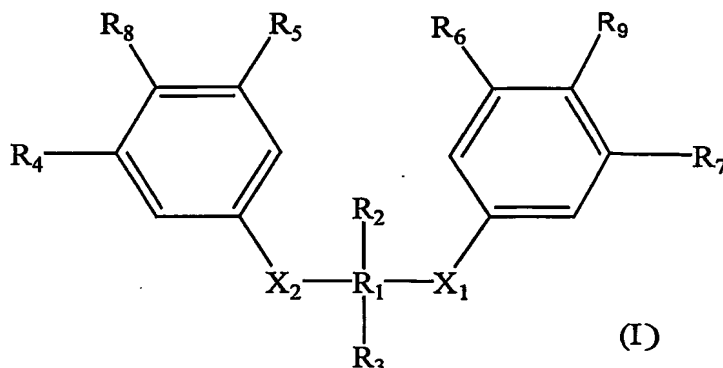


WHAT IS CLAIMED:

1. A method for the prophylactic or therapeutic treatment of a disease or disorder associated with vascular health, said method comprising administering to a subject in need of such treatment an amount effective to treat a disease or disorder associated with vascular health, of a compound of Formula (I):



wherein:

X₁ and X₂ are independently selected from the group consisting of oxy and a dialkyl substituted silyl;

R₁ is C₁-C₄ alkyl;

R₂ and R₃ are independently selected from the group consisting of H and a C₁-C₄ alkyl;

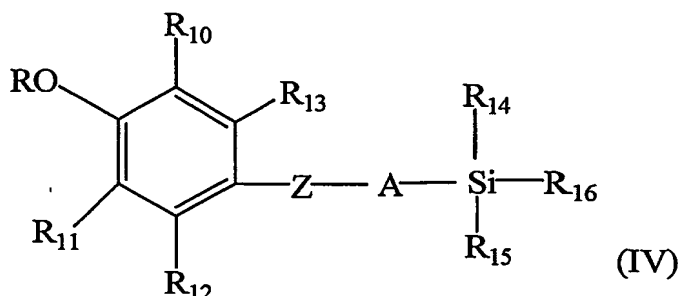
R₄, R₅, R₆, and R₇ are independently selected from the group consisting of H, methoxy, and a branched or straight chain C₁-C₆ alkyl; and

R₈ and R₉ are independently selected from the group consisting of hydrogen, hydroxy, trifluoromethyl, halide, amine, alkyl, alkenyl, aryl, heteroaryl, alkanoyl, aryloyl, heteroaryloyl, -O(C₁-C₆ alkyl), -OCO-(H or C₁-C₇ alkyl), -OCO-(C₃-C₇ alkenyl), -OCO-(aryl), -OCO-(heteroaryl), -(C₀-C₈ alkyl)-COOH, -(C₂-C₈ alkenyl)-COOH, -OCO-(C₀-C₆ alkyl)-COOH, -OCO-(C₂-C₆ alkenyl)-COOH, -CO-(C₀-C₆ alkyl)-COOH, and -CO-(C₂-C₆ alkenyl)-COOH;

wherein when the R₈ or R₉ substituents are alkyl, alkenyl, aryl, heteroaryl, alkanoyl, aryloyl, heteroaryloyl, -O(C₁-C₆ alkyl), -OCO-(H or C₁-C₇ alkyl), -OCO-(C₃-C₇ alkenyl), -OCO-(aryl), -OCO-(heteroaryl), -(C₀-C₈ alkyl)-COOH, -(C₂-C₈ alkenyl)-COOH, -OCO-(C₀-C₆ alkyl)-COOH, -OCO-(C₂-C₆ alkenyl)-COOH, -CO-

(C₀-C₆ alkyl)-COOH, or -CO-(C₂-C₆ alkenyl)-COOH, they may be independently substituted with one or more functionalities independently selected from the group consisting of C₁-C₆ alkyl, halogen, -OH, -OCH₃, -OCH₂CH₃, halomethyl, dihalomethyl, trihalomethyl, -NH₂, -NO₂, -CN, -NC, -C(=NH)(-NH₂), -SH, -COOH, -COOCH₃, and -COOCH₂CH₃;

with the proviso that said compound of Formula (I) is not a compound of Formula (IV)



wherein:

R₁₀ and R₁₅ are each independently C₁ - C₆ alkyl;

R₁₁, R₁₂ and R₁₃ are each independently hydrogen or C₁ - C₆ alkyl;

R is hydrogen or -C(O)-(CH₂)_m-Q, wherein Q is hydrogen or -COOH and m is an integer 1, 2, 3 or 4;

Z is a thio, oxy or methylene group;

A is a C₁ - C₄ alkylene group;

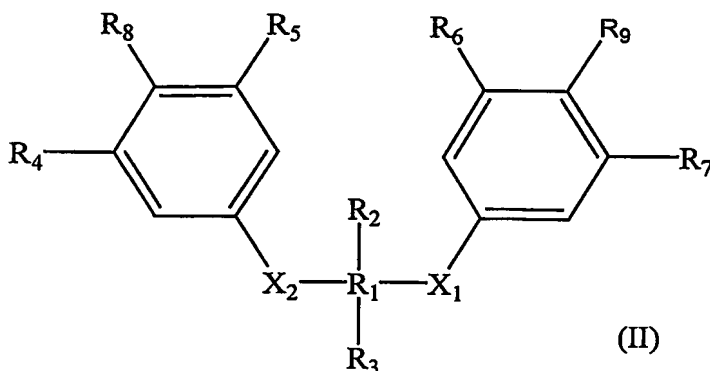
R₁₄ and R₁₆ are each independently a C₁ - C₆ alkyl or -(CH₂)_n-(Ar), wherein n is an integer 0, 1, 2 or 3; and Ar is phenyl or naphthyl unsubstituted or substituted with one to three substituents selected from the group consisting of hydroxy, methoxy, ethoxy, halogen, trifluoromethyl, C₁ - C₆ alkyl, or -NR₁₇ R₁₈, wherein R₁₇ and R₁₈ are each independently hydrogen or C₁ - C₆ alkyl; with the proviso that when R₁₁ and at least one of R₁₄ or R₁₆ is C₁ - C₆ alkyl, and Ar is not substituted with trifluoromethyl or -NR₁₇ R₁₈, then R is -C(O)-(CH₂)_m-Q; or a pharmaceutically acceptable salt thereof.

2. The method of claim 1, wherein X₁ and X₂ are independently selected from the group consisting of oxy and dimethyl-silyl; R₁ is methylene; R₂ and R₃ are hydrogen, R₄, R₅, R₆, and R₇ are independently selected from the group consisting of

hydrogen and tert-butyl; and R_8 and R_9 are independently selected from the group consisting of hydroxy and methoxy.

3. The method of claim 1, wherein R_4 and R_5 are tert-butyl, and R_8 is hydroxy.

5 4. A method for the prophylactic or therapeutic treatment of a disease or disorder associated with vascular health, said method comprising administering to a subject in need of such treatment an amount effective to treat a disease or disorder associated with vascular health, of a compound of Formula (II):



10 wherein

X_1 and X_2 are independently selected from the group consisting of thio, oxy, and a dialkyl substituted silyl;

R_1 is C_1 - C_4 alkyl;

15 R_2 and R_3 are independently selected from the group consisting of H and a C_1 - C_4 alkyl;

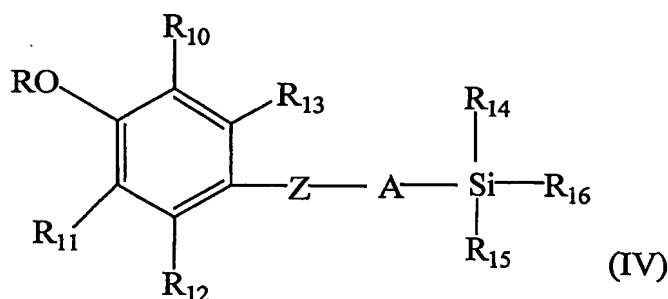
R_4 , R_5 , R_6 , and R_7 are independently selected from the group consisting of H, methoxy, and a branched or straight chain C_1 - C_6 alkyl; and

20 R_8 and R_9 are independently selected from the group consisting of hydrogen, hydroxy, trifluoromethyl, halide, amine, alkyl, alkenyl, aryl, heteroaryl, alkanoyl, aryloyl, heteroaryloyl, $-O(C_1$ - C_6 alkyl), $-OCO$ -(H or C_1 - C_7 alkyl), $-OCO$ -(C_3 - C_7 alkenyl), $-OCO$ -(aryl), $-OCO$ -(heteroaryl), $-(C_0$ - C_8 alkyl)- $COOH$, $-(C_2$ - C_8 alkenyl)- $COOH$, $-OCO$ -(C_0 - C_6 alkyl)- $COOH$, $-OCO$ -(C_2 - C_6 alkenyl)- $COOH$, $-CO$ -(C_0 - C_6 alkyl)- $COOH$, and $-CO$ -(C_2 - C_6 alkenyl)- $COOH$;

25 wherein when the R_8 or R_9 substituents are alkyl, alkenyl, aryl, heteroaryl, alkanoyl, aryloyl, heteroaryloyl, $-O(C_1$ - C_6 alkyl), $-OCO$ -(H or C_1 - C_7 alkyl), $-OCO$ -

(C₃-C₇ alkenyl), -OCO-(aryl), -OCO-(heteroaryl), -(C₀-C₈ alkyl)-COOH, -(C₂-C₈ alkenyl)-COOH, -OCO-(C₀-C₆ alkyl)-COOH, -OCO-(C₂-C₆ alkenyl)-COOH, -CO-(C₀-C₆ alkyl)-COOH, or -CO-(C₂-C₆ alkenyl)-COOH, they may be independently substituted with one or more functionalities independently selected from the group consisting of C₁-C₆ alkyl, halogen, -OH, -OCH₃, -OCH₂CH₃, halomethyl, dihalomethyl, trihalomethyl, -NH₂, -NO₂, -CN, -NC, -C(=NH)(-NH₂), -SH, -COOH, -COOCH₃, and -COOCH₂CH₃;

with the proviso that when said compound of Formula (II) is not a compound of Formula (IV)



wherein:

R₁₀ and R₁₅ are each independently C₁ - C₆ alkyl;

R₁₁, R₁₂ and R₁₃ are each independently hydrogen or C₁ - C₆ alkyl;

R is hydrogen or -C(O)-(CH₂)_m-Q, wherein Q is hydrogen or -COOH and

m is an integer 1, 2, 3 or 4;

Z is a thio, oxy or methylene group;

A is a C₁ - C₄ alkylene group;

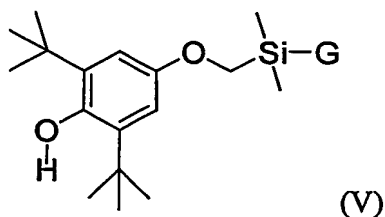
R₁₄ and R₁₆ are each independently a C₁ - C₆ alkyl or -(CH₂)_n-(Ar), wherein n is an integer 0, 1, 2 or 3; and Ar is phenyl or naphthyl unsubstituted or substituted with one to three substituents selected from the group consisting of hydroxy, methoxy, ethoxy, halogen, trifluoromethyl, C₁ - C₆ alkyl, or -NR₁₇R₁₈, wherein R₁₇ and R₁₈ are each independently hydrogen or C₁ - C₆ alkyl; with the proviso that when R₁₁ and at least one of R₁₄ or R₁₆ is C₁ - C₆ alkyl, and Ar is not substituted with trifluoromethyl or -NR₁₇R₁₈, then R is -C(O)-(CH₂)_m-Q; or a pharmaceutically acceptable salt thereof.

5. The method of claim 4, wherein X_1 and X_2 are independently selected from the group consisting of thio and dimethyl-silyl; R_1 is methylene; R_2 and R_3 are independently selected from the group consisting of hydrogen and methyl; R_4 , R_5 , R_6 , and R_7 are independently selected from the group consisting of hydrogen and tert-butyl; and R_8 and R_9 are independently selected from the group consisting of hydrogen, hydroxy, methoxy, and butandioate; with the proviso that when X_1 and X_2 are both thio, R_8 and R_9 are not both hydroxy.

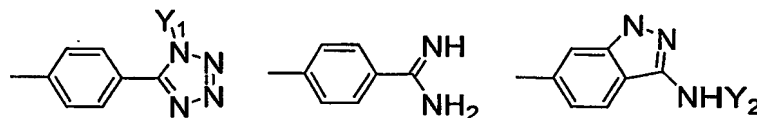
6. The method of claim 4, wherein R_4 and R_5 are tert-butyl, and R_8 is hydroxy.

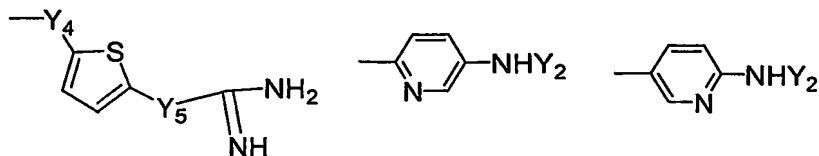
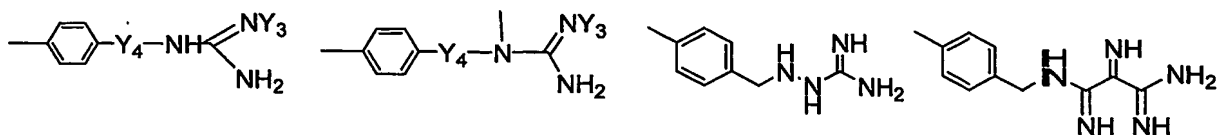
7. The method of claim 4, wherein X_1 and X_2 are thio; R_1 is methylene; R_2 and R_3 are methyl; R_4 , R_5 , R_6 , and R_7 are tert-butyl; R_8 is hydroxy; and R_9 is butandioate.

8. A method for the prophylactic or therapeutic treatment of a disease or disorder associated with vascular health, said method comprising administering to a subject in need of such treatment an amount effective to treat a disease or disorder associated with vascular health, of a compound of Formula (V):

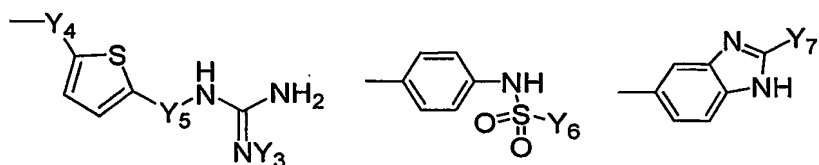
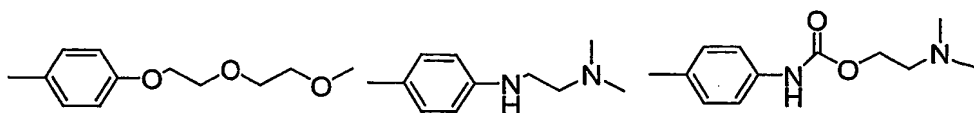


wherein G is selected from the group consisting of:

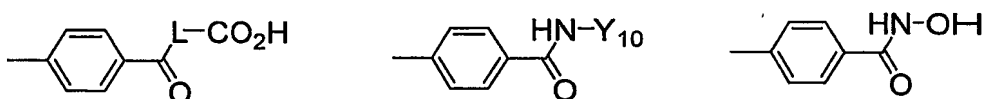




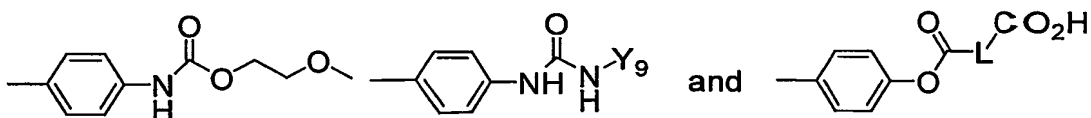
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wherein:

Y₁ is -H, C₁-C₄ alkyl, or C₃-C₆ alkenyl;

20 Y₂ is -H, C₁-C₄ alkyl, or C₃-C₆ alkenyl, aryl, heteroaryl, aryloyl, alkanoyl, or heteroaryloyl;

Y₃ is -H, -CN, C₁-C₄ alkyl, C₃-C₆ alkenyl, aryl or heteroaryl;

Y₄ is (CH₂)_n, where n is 0-4, or C₂-C₆ alkenyl;

Y₅ is NH, (CH₂)_n, where n is 0-4, or C₂-C₆ alkenyl;

25 Y_6 is C₁-C₄ alkyl, C₃-C₆ alkenyl, aryl, heteroaryl, alkylaryl, or alkylheteroaryl;

Y₇ is H, C₁-C₄ alkyl, C₃-C₆ alkenyl, aryl, heteroaryl, alkylaryl, or alkylheteroaryl, or NH Y₈;

Y_8 is C_1 - C_4 alkyl, C_3 - C_6 alkenyl, aryl, heteroaryl, alkylaryl, or alkylheteroaryl;

Y_9 is C_1 - C_4 alkyl, C_3 - C_6 alkenyl, aryl, or heteroaryl;

Y_{10} is alkyl, aryl, heteroaryl, alkylaryl, or alkylheteroaryl;

L is C_1 - C_6 alkyl or C_2 - C_6 alkenyl; and

- 5 wherein G may be additionally substituted with one or more substituents independently selected from the group consisting of -F, -Cl, -Br, -I, -NH₂, -OH, -CN, -SH, -CH₃, -CH₂CH₃, -CF₃, -OCH₃, -OCH₂CH₃, -COOH, -COOCH₃, and -COOCH₂CH₃.

9. A method according to any of claims 1 to 8, wherein said disease or
10 disorder associated with vascular health is selected from the group consisting of: major adverse cardiac events, vascular access dysfunction, and male erectile dysfunction.

10. A method according to any of claims 1 to 9, wherein said subject is
15 selected from the group consisting of a hemodialysis patient, an end stage renal disease patient, or a diabetic patient.

11. A method according to any of claims 1 to 10, wherein said subject is a subject having an increased oxidative burden or elevated oxidative stress, a subject having a vascular access shunt or graft, or a subject suffering from diabetes and experiencing erectile dysfunction or seeking prophylactic therapy.

- 20 12. A method according to any of claims 1 to 11, wherein said subject is a human.

13. A method according to any of claims 1 to 12, wherein said compound is administered to the subject orally.

- 25 14. A method according to any of claims 1 to 13, wherein about 1mg to about 10g of said compound is administered per day to said subject in single, divided, or continuous doses to achieve a blood plasma concentration of said compound which is therapeutically effective in said treatment.

15. A method according to any of claims 1 to 13, wherein about 0.1g to about 3g of said compound is administered per day to said subject in single, divided, or continuous doses to achieve a blood plasma concentration of said compound which is prophylactically effective in said treatment.

5 16. A method according to any of claims 1 to 8, wherein said disease or disorder associated with vascular health is a major adverse cardiac event.

17. The method of claim 16, wherein said subject is a subject having an increased oxidative burden or elevated oxidative stress.

10 18. The method of claim 16, wherein treatment includes a reduction in the risk of occurrence of said major adverse cardiac event.

19. The method of claim 16, wherein said method comprises identifying a subject as having an increased oxidative burden or elevated oxidative stress.

20. The method of claim 16, wherein said subject has normal or normalized lipid levels.

15 21. A method according to any of claims 1 to 8, wherein said disease or disorder associated with vascular health is vascular access dysfunction.

22. The method of claim 21, wherein said subject is a hemodialysis patient and said compound is administered directly following hemodialysis.

20 23. The method of claim 21, wherein said subject suffers from end stage renal disease.

24. The method of claim 21, wherein said vascular access dysfunction is associated with arteriovenous shunt stenosis.

25. A method according to any of claims 1 to 8, wherein said disease or disorder associated with vascular health is erectile dysfunction.

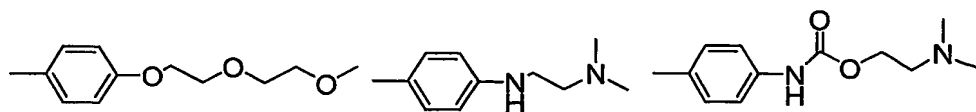
25 26. The method of claim 25, wherein said subject is a diabetic suffering from erectile dysfunction.

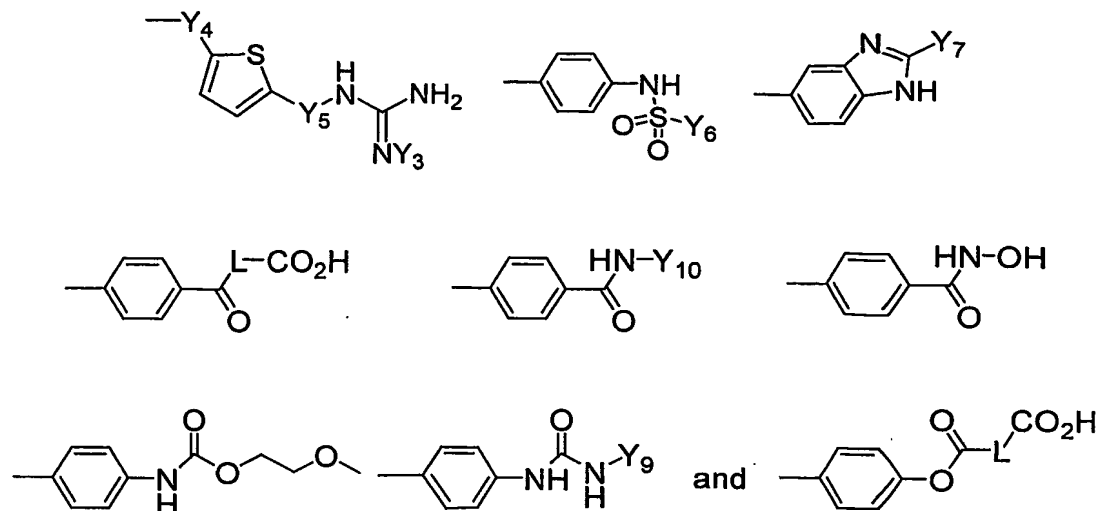
28. The method of claim 25, wherein said treatment is a combination treatment comprising a phosphodiesterase inhibitor as a second active ingredient.

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wherein:

- 10 Y_1 is $-H$, C_1 - C_4 alkyl, or C_3 - C_6 alkenyl;
 Y_2 is $-H$, C_1 - C_4 alkyl, or C_3 - C_6 alkenyl, aryl, heteroaryl, aryloyl, alkanoyl, or heteroaryloyl;
 Y_3 is $-H$, $-CN$, C_1 - C_4 alkyl, C_3 - C_6 alkenyl, aryl or heteroaryl;
 Y_4 is $(CH_2)_n$, where n is 0-4, or C_2 - C_6 alkenyl;
15 Y_5 is NH , $(CH_2)_n$, where n is 0-4, or C_2 - C_6 alkenyl;
 Y_6 is C_1 - C_4 alkyl, C_3 - C_6 alkenyl, aryl, heteroaryl, alkylaryl, or alkylheteroaryl;
 Y_7 is H , C_1 - C_4 alkyl, C_3 - C_6 alkenyl, aryl, heteroaryl, alkylaryl, or alkylheteroaryl, or NH Y_8 ;
 Y_8 is C_1 - C_4 alkyl, C_3 - C_6 alkenyl, aryl, heteroaryl, alkylaryl, or alkylheteroaryl;
20 Y_9 is C_1 - C_4 alkyl, C_3 - C_6 alkenyl, aryl, or heteroaryl;
 Y_{10} is alkyl, aryl, heteroaryl, alkylaryl, or alkylheteroaryl;
 L is C_1 - C_6 alkyl or C_2 - C_6 alkenyl; and
wherein G may be additionally substituted with one or more substituents independently selected from the group consisting of $-F$, $-Cl$, $-Br$, $-I$, $-NH_2$, $-OH$, $-CN$, $-SH$, $-CH_3$, $-CH_2CH_3$, $-CF_3$, $-OCH_3$, $-OCH_2CH_3$, $-COOH$, $-COOCH_3$, and $-COOCH_2CH_3$;
25 and a pharmaceutically acceptable excipient.

30. The pharmaceutical composition of claim 29, wherein said compounds of Formula (V) are formulated for oral administration in a self-emulsifying drug delivery system.

31. The pharmaceutical composition of claim 29, further comprising one or members of the group consisting of lactose, calcium phosphate, kaolin, glycerin, propylene glycol, polyethylene glycol, peanut oil, liquid paraffin, olive oil, sodium carboxymethylcellulose, methylcellulose, hydroxypropyl methylcellulose, sodium alginate, polyvinylpyrrolidone, gum tragacanth, gum acacia; dispersing agents, wetting agents, and thickening agents.

32. The pharmaceutical composition of any one of claims 29 to 31, further comprising one or more other active ingredients useful in the prophylactic or therapeutic treatment of major adverse cardiac events.

33. The pharmaceutical composition of any one of claims 29 to 31, further comprising one or more other active ingredients useful in the prophylactic or therapeutic treatment of vascular access dysfunction.

34. The pharmaceutical composition of any one of claims 29 to 31, further comprising one or more other active ingredients useful in the prophylactic or therapeutic treatment of erectile dysfunction.